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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,861	02/07/2002	Kevin M. Slawin	675.002US1	1421

21186 7590 08/05/2005

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EXAMINER	
NEGIN, RUSSELL SCOTT	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 08/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,861	SLAWIN ET AL.	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-36* is/are pending in the application.

4a) Of the above claim(s) *1-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-36* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/27/03, 5/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of claims 28-36 (Group V) in the reply filed on May 2, 2005 is acknowledged. The traversal is on the ground(s) that the inventions stated are closely related. This is not found persuasive because each protein in the group consisting of TGF-β1, IGFBP-2, IGFBP-3, IL-6, and IL-6sR results in unique progression free probability profiles of prostate cancer. Additionally, growth factors, growth factor binding proteins, and interleukins play different physiological roles in mammals. While interleukins can affect cell growth, transforming growth factors are a much broader and more diverse class of proteins. Thus, each group is considered distinct as independent inventions. The requirement is still deemed proper and is therefore made FINAL.

interleukin
Definition:

Any of a group of protein factors which are produced by T lymphocytes and macrophages (a type of white blood cell) in the presence of antigens or mitogens. They cause the T lymphocytes to activate and proliferate
Biotech Life Sciences Dictionary © 1995-1998

Transforming Growth Factor-Beta (TGF-beta)
An angiogenic growth factor produced by tumor cells, it is able to induce specific malignant characteristics in normal cells (such as fibroblasts), thereby "transforming" those cells from epithelial phenotype to mesenchymal phenotype (thereby enabling cell motility).

Biotech terms online glossary www.biotech.org

Specification

The abstract of the disclosure is objected to because the abstract is shorter than the recommended length of 50 to 150 words. Correction is required. See MPEP § 608.01(b).

In addition, although the abstract should be a concise statement of technical disclosure, it should reveal in more detail what is new in the art besides the objective or utility of the innovation. Allusions to growth factors or interleukins and their roles in prostate cancer and prostate cancer metastasis may prove to be helpful for a more informative description.

Claim Rejections - 35 USC § 112

Claims 28-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for prostate cancer and cancer originating from the prostate, does not reasonably provide enablement for other disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to duplicate invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction presented, (3) the presence or absence of working examples,

(4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount of prima facia case are discussed below.

The aforementioned eight factors can be addressed as follows:

(1) There is undue quantity of experimentation needed to assess all the types of disease claimed in Claims 28-36. It is unpredictable that the same growth factors accounted in the claims can be applied in experimentally the same manner to unrelated ailments.

(2) There is sufficient lack of direction presented for diseases besides prostate cancer and cancer metastasis presented in the specification to make the application of this invention to other diseases unpredictable.

(3) There are four relevant working examples provided in the disclosure for prostate cancer and prostate cancer metastasis. However, there are no working examples for other diseases.

(4) The nature of the invention is directed to prostate cancer and metastases originating from the prostate. The act of determining disease prognoses is complex, especially for prostate cancer.

(5) The diverse prior art for determining the prognoses of many types of disease suggests there is no homogeneous method of determining the prognosis for all diseases pertaining to level of growth factor in the body.

(6) The relative skill of those in the art suitable to comprehend and execute this invention is a graduate degree in biotechnology or medical degree.

(7) There are vast amounts of research used by doctors to diagnose and give prognoses for certain diseases; this research can be complex and vary with the type of disease. It is unpredictable that a method used in this disease can be applied to other ailments.

(8) The claims are broad; use of growth factor covers any disease. The breadth of the claims are much broader than the scope of enablement in the disclosure. Thus, it puts undue burden on one skilled in the art to apply the results of this study to predictably use the disclosed information for other diseases.

Claims 28 and 29 claim that the apparatus will provide a risk of disease progression in the mammal; the patent application examines and analyzes specifically prostate cancer and cancer originating from the prostate and no other disease. Claims 30-33 are dependent from the apparatus in claims 28 or 29; this apparatus comprises software which provides the risk of disease progression in mammals, the apparatus of claims 30-33 are not enabled for diseases other than prostate cancer for reasons discussed below. Claims 34-35 provide a method of prognosis of prostate cancer in patients after therapy. Part (c) of claim 34 claims that analysis of the test information provides the "risk of disease progression" in the patient. Again, this method is enabled

for prostate cancer and no other disease. Part (c) of claim 35 and claim 36 claim that analyses of the test information provide "risk of non-prostate confined disease" in the patient. The inventors do not describe which non-prostate confined disease is germane to this application.

An example of a disease with which distant prostate cancer metastasis is uncorrelated is with male pattern baldness (baldness or alopecia is defined in Stedman's Medical dictionary as a disease resulting in the absence or loss of hair). Inhibition of hair growth is related to testosterone levels in the body (Noriko and Hideo, Endocrinology, vol 138, 1997, pp. 356-361; Ebling FJ, Clinical Endocrinology Metabolism, vol. 15, 1986, 319-339). However, serum testosterone levels were found not to be related to distant metastasis of cancer in the prostate (Kelly et al., Urologic Oncology, 2000, vol 5, pp. 78-84). Kelly et al. found that "serum testosterone did not correlate with palpable stage, Gleason score, pretreatment PSA, or lymph node involvement." Thus, this is an instance where disease progression of alopecia is unrelated to prostate cancer metastasis; it is unpredictable that the claimed proteins result in diseases (i.e. alopecia) other than those studied in the specifications.

A second relevant example is sickle cell anemia. This disease results from a single amino acid mutation in hemoglobin. This mutation results from a mistake in the genes encoding hemoglobin and has nothing in common with levels of the listed growth factors and interleukins in the claims. It is unpredictable that the claimed proteins result in diseases (i.e. sickle cell anemia) other than those studied in the specifications.

The eight factors reiterated in In re Wands confirm that a much more complex system would be required along with undue experimentation to give prognoses for all the types of diseases claimed by the applicant. The specification is only linked to the claimed growth factor as to the level and art with prostate cancer and its metastasis. Thus, the application is enabled for prostate cancer and its metastasis and no other disease.

Claims 28-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for humans, does not reasonably provide enablement for other mammals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount of prima facia case are discussed below.

The specifications disclose information with the human species as its only source of data, yet the claims state that the apparatus is relevant for all mammalian species. The Claims 34-36 do not directly specify that the "patient" is human. Although animals are frequently used to test treatments for human diseases, there are significant differences, especially in types of cancer between humans and other mammals. For example, Adachi and Takemoto, compare lung cancer between humans and lab animals and find that the characteristics of lung tumors occurring in animals are rather different from those occurring in humans (Sangyo igaku. Japanese journal of industrial health, 1987, vol 29, pp. 345-357, abstract). Furthermore, Mauderly shows that the pulmonary responses of rats to dusts and thus rate of cancer development differ from other rodents and humans (Symposium on silica, silicosis, and cancer, San Francisco, CA; October 28-30, 1993, abstract). Thus it is unprecitable to apply the same result for a human to other mammalian species.

Claims 28-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for each of the protein individually, does not reasonably provide enablement for combinations of the declared proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to duplicate the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount of prima facia case are discussed below.

Claims 28 and 29 use the terminology "at least one protein" in a sample (sample is defined in the specifications on page 4). While the invention is enabled for single species of proteins listed in Claims 28, 29, or 32; the said terminology can imply correlations with combinations of protein molecules. Combinations of proteins (i.e. growth factors) are not investigated in the application; they are investigated individually. For example, combinations of drugs can change the efficiency of individual chemicals (Antonello, Ph.D. Thesis, Temple University, 1996, abstract). Lamy and Kitler wrote a review on the subject of dangerous drug interactions (Diseases of the Nervous System, 1971, vol. 32, pp. 17-23.) Yip et al. elaborate on the specific topic of the adverse effect of topical methylsalicylate ointment on warfarin anticoagulation (Yip et al., Postgraduate

medical journal (UK), 1990, vol 66, pp. 367-369). For the example of TGF-beta1, Tirone ey al. find hyaluronan synthesis to be regulated by a combination of epidermal growth factor and TGF-beta1 (Tirone et al., The Journal of Biological Chemistry, vol 272, 1997, 4787). Thus, results of combinations are unpredictable in that growth factors can augment or regulate each other in the form of interactions that can be cooperative or uncooperative.

Claims 28, 29, 32, 34, 35, and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims make use of abbreviations difficult for one skilled in the art to distinctly resolve. An example is TGF-β1 which represents transforming growth factor- beta 1.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Ardin Marschel, Ph.D., Supervisory Patent Examiner, can be reached at (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

July 14, 2005

Ardin H. Marschel 7/15/05

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER